UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,347	06/26/2002	Leonard C.W. Seymour	P 0284085	3808

909 7590 03/10/2005

PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,347	SEYMOUR ET AL.	
	Examiner	Art Unit	
	Gerald G. Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-9* is/are rejected.

7)☒ Claim(s) *4 and 10-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/26/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-30) in the reply filed on 12/20/2004 is acknowledged. The traversal is on the ground(s) that the teachings of U.S. Patent No. 5,521,291 do not anticipate the claimed invention and that there is unity of invention amongst the different groups. This argument is found to be persuasive because the '291 patent does not teach a polymer-modified biological element as is recited in the first claim of Group I. The restriction requirement was predicated on an interpretation of the term "biological element" as encompassing proteins such as the modified antibody taught in the '291 patent. Upon further review of the instant specification, it is apparent that applicants have limited the term "biological element" to encompass only bacteria, bacteriophages, fungi, spores (from bacteria or fungi), viruses and viral cores (see page 4, lines 24-28 of the instant specification).

In view of this definition and applicants arguments in the response filed 12/20/2004, Groups I-III are REJOINED. Claims 1-31 are pending and under consideration in the instant application.

Claim Objections

Claims 4, 10-24, 26-31 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiply dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the

claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 25 is in improper dependent form because it claims dependency from itself. Claim 25 has not been further examined on the merits as it is impossible to determine what limitations were intended to be incorporated into the claim by dependency.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 & 5-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3 and 5 are directed to methods of modifying the biological and/or physiochemical properties of a biological element, the method comprising reacting the biological element with a multivalent polymer having multiple reactive groups so that the biological element is linked to the polymer by a plurality of covalent linkages and is thereby modified such that biological and/or physiochemical properties of the biological element are altered. Claims 6-9 are directed to a polymer modified biological element in which the biological element is covalently linked to a polymer having multiple reactive groups such that said polymer is linked to the biological element by at least two covalent linkages and whereby biological and/or

physiochemical properties of the biological element are modified. The specification defines the term "biological element" to encompass only bacteria, bacteriophages, fungi, spores (from bacteria or fungi), viruses and viral cores. The specification clarifies that the term "viral core" refers to a virus that has been treated so as to have an outer surface envelope or capsid of the virus removed (see page 4, lines 24-28 of the instant specification). The specification teaches that changes or modifications of biological or physiochemical properties can include alteration of the protein interactions the biological element would normally have in the absence of the multivalent polymer (e.g. change in tropism for a particular cell type), changes in solubility or partition co-efficient. The biological element can comprise "therapeutic genetic material".

A critical element of the invention is the multivalent polymer used to modify or alter the biological element of the invention through its attachment via a plurality of covalent linkages. The rejected claims encompass an enormously broad genus of such multivalent polymers that includes literally any multivalent polymer of any type that must be retain the function of forming a complex with literally any type of bacterial cell, viral particle, bacteriophage or spore where the multivalent polymer forms at least two covalent linkages and where the addition of the multivalent polymer alters at least one biological or physiochemical property of the biological element. The instant specification teaches only a few working examples built around multivalent polymers having an N-2-hydroxypropylmethylacrylamide (HPMA), N-(2-hydroxyethyl)-1-glutamine (HEG) or ethylenglycol-oligopeptide backbone. No other multivalent polymer having a different structural backbone is described. Thus, there is no means for the skilled artisan to envision other types of multivalent polymers that will necessarily retain the function of forming multiple covalent linkages with at least one type of biological element and where formation of

the complex will necessarily result in a change in at least one biological and/or physiochemical property of the biological element.

The prior art does not appear to offset the deficiencies of the instant specification. The prior art does not appear to teach the use of a multivalent polymer that forms multiple covalent linkages per polymer molecule with a biological element to modify the biological or physiochemical properties of a bacterial cell, viral particle, bacteriophage or spore.

Given the enormous genus of multivalent polymers encompassed by the rejected claims and the lack of description in the specification or prior art of a sufficient number of specific embodiments of such multivalent polymers so as to describe the broadly claimed genus, the skilled artisan would reasonably have concluded that applicants were not in possession of the broadly claimed invention.

Claims 1-3 & 5-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for embodiments where the backbone of the multivalent polymer is N-2-hydroxypropylmethylacrylamide (HPMA), N-(2-hydroxyethyl)-1-glutamine (HEG) or ethyleneglycol-oligopeptide backbone, does not reasonably provide enablement for embodiments where the multivalent polymer is derived from a different polymer backbone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of

experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: Claims 1-3 and 5 are directed to methods of modifying the biological and/or physiochemical properties of a biological element, the method comprising reacting the biological element with a multivalent polymer having multiple reactive groups so that the biological element is linked to the polymer by a plurality of covalent linkages and is thereby modified such that biological and/or physiochemical properties of the biological element are altered. Claims 6-9 are directed to a polymer modified biological element in which the biological element is covalently linked to a polymer having multiple reactive groups such that said polymer is linked to the biological element by at least two covalent linkages and whereby biological and/or physiochemical properties of the biological element are modified. The specification defines the term "biological element" to encompass only bacteria, bacteriophages, fungi, spores (from bacteria or fungi), viruses and viral cores. The specification clarifies that the term "viral core" refers to a virus that has been treated so as to have an outer surface envelope or capsid of the virus removed (see page 4, lines 24-28 of the instant specification). The invention is complex, involving the covalent attachment of a single polymeric molecule to at least two sites on the surface of a biological element in such a way that at least one biological or physiochemical property of the biological element (e.g. phage, virus or bacterial cell) is altered.

Breadth of the claims: The complex nature of the invention is exacerbated by the great breadth of possible multivalent polymers encompassed by the rejected claims and the functional limitations of the claims with regard to attachment of the polymer to the biological element and

with regard to the types of alterations in biological and/or physiochemical properties contemplated by the specification.

Guidance of the specification/The existence of working examples: The teachings of the specification are directed to the use of multivalent polymers where the polymer has an N-2-hydroxypropylmethylacrylamide (HPMA), N-(2-hydroxyethyl)-1-glutamine (HEG) or ethyleneglycol-oligopeptide backbone. Several working examples are provided where an HPMA-based polymer is added to different biological elements (e.g. adenovirus, vaccinia virus, bacculovirus, Pseudomonas sp., etc.) to alter their biological and/or physiochemical properties (e.g. tropism, enhanced solubility in non-aqueous solvents, etc..). No significant guidance is provided, however, for the development of multivalent polymers for use in generating altered biological elements where the backbone is not derived from N-2-hydroxypropylmethylacrylamide (HPMA), N-(2-hydroxyethyl)-1-glutamine (HEG) or an ethyleneglycol-oligopeptide.

State of the art/Predictability of the art: The concept of using the type of multivalent polymer taught in the instant specification to generate an altered biological element through multiple covalent linkages per molecule of polymer appears to have been novel in the art at the time of filing. For example, WO 98/44143 teaches several different methods for modifying a virus particle through covalent linkage to polyethylene glycol (PEG) (e.g. Abstract, Example 11, pages 35-36). However, each of the prior art references cited in the international search report for this application that teach the "PEGylation" of viral particles appears to teach the covalent attachment of PEG to the particle through a single covalent bond. This appears to be due to the chemical structure of PEG [$H(OCH_2CH_2)_nOH$], which has a limited number of reactive groups

(e.g. page 6; Example 11; etc. of WO 98/44143). Therefore, the prior art does not provide significant guidance with regard to adapting other type of polymer backbones for use in making the recited biological elements having a multivalent polymer attached by at least two covalent bonds. Thus, it would've required trial and error experimentation of an inventive nature for the skilled artisan to develop other types of multivalent polymer backbones for the alteration of the biological and/or physiochemical properties of biological elements at the time of the invention.

The amount of experimentation necessary:

Given the combination of factors outlined above, it would have taken undue and unpredictable experimentation in order to practice the claimed invention in the full, broad scope encompassed by the rejected claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-3 & 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "change or modify" are unclear. It is unclear the difference between the two terms "change" and "modify" since the words are synonymous.

Regarding claim 3, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are *necessarily* part of the claimed invention. See MPEP § 2173.05(d).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G. Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

ggl

GERRY LEFFERS
PRIMARY EXAMINER